

WHAT IS CLAIMED IS:

1 1. An isolated nucleic acid encoding a Slo4 polypeptide comprising
2 an alpha subunit of a Slo potassium channel, the polypeptide:
3 (i) forming, with at least one additional alpha subunit, a potassium
4 channel comprising the characteristic of voltage-gating; and
5 (ii) hybridizing under stringent hybridization conditions to a
6 nucleic acid encoding a polypeptide comprising an amino acid sequence of SEQ ID
7 NO:4, wherein the hybridization reaction is incubated at 42°C in a solution comprising
8 50% formamide, 5x SSC, and 1% SDS, and washed at 65°C in a solution comprising 0.2x
9 SSC and 0.1% SDS.

1 2. The nucleic acid of claim 1, wherein the polypeptide specifically
2 binds to antibodies generated against SEQ ID NO:4.

1 3. The nucleic acid of claim 1, wherein the potassium channel further
2 comprises the characteristic of rapid activation.

1 4. The nucleic acid of claim 1, wherein the nucleic acid encodes a
2 polypeptide comprising an amino acid sequence of SEQ ID NO:4.

1 5. The nucleic acid of claim 1, wherein the nucleic acid comprises a
2 nucleotide sequence of SEQ ID NO:3.

1 6. The nucleic acid of claim 1, wherein the nucleic acid is amplified
2 by at least one pair of primers that selectively hybridize under stringent hybridization
3 conditions to the same sequence as the primers selected from the group consisting of:

4 5'-GGCGTCTGCTTGATTGGTGTAGGA-3' (SEQ ID NO:23)

5 5'-ATCAAAGTTGAGTTTCCTCCCGAG-3' (SEQ ID NO:24)

6 5'-CCCGGAGCATCTACCGTACATCTTC-3' (SEQ ID NO:25)

7 5'-CCAGCTGTTCAAAGTGTATGGGTAG-3' (SEQ ID NO:26)

8 5'-GCTTGGAGGACCATGTTTCAGGAGT-3' (SEQ ID NO:27)

9 5'-ATGGTTGATTTGGAGAGCGAAGTG-3' (SEQ ID NO:28)

10 5'-CAATTTTGAGAGCATGGGCTGTGAAAG-3' (SEQ ID NO:29)

11 5'-GACTTATGGATCAGAACTTATGCCCAG-3' (SEQ ID NO:30)

12 5'-CATCTGGTGTAGTTTCATCTTCTGATTGG-3' (SEQ ID NO:31).

1 7. The nucleic acid of claim 1, wherein the polypeptide encoded by
2 the nucleic acid comprises an alpha subunit of a homomeric potassium channel.

1 8. The nucleic acid of claim 1, wherein the polypeptide encoded by
2 the nucleic acid comprises an alpha subunit of a heteromeric potassium channel.

1 9. The nucleic acid of claim 1, wherein the nucleic acid encodes a
2 polypeptide comprising a sequence having at least 60% amino acid sequence identity to
3 an amino acid sequence of SEQ ID NO:4.

1 10. An isolated nucleic acid that specifically hybridizes under
2 moderately stringent conditions to a nucleic acid encoding an amino acid sequence of
3 SEQ ID NO:4, wherein the hybridization conditions include incubation at 37°C in a
4 solution comprising 40% formamide, 1 M NaCl, 1% SDS at, and a wash at 45°C in a
5 solution comprising 1X SSC.

1 11. A method of detecting a nucleic acid, the method comprising
2 contacting the nucleic acid with an isolated nucleic acid of claim 1.

1 12. An isolated Slo4 polypeptide comprising an alpha subunit of a Slo
2 potassium channel, the polypeptide:

3 (i) forming, with at least one additional alpha subunit, a potassium
4 channel comprising the characteristic of voltage-gating; and

5 (ii) encoded by a nucleic acid sequence that hybridizes under
6 highly stringent hybridization conditions to a nucleic acid encoding a polypeptide
7 comprising an amino acid sequence of SEQ ID NO:4, wherein the hybridization reaction
8 is incubated at 42°C in a solution comprising 50% formamide, 5x SSC and 1% SDS, and
9 washed at 65°C in a solution comprising 0.2x SSC and 0.1% SDS.

1 13. The polypeptide of claim 12, wherein the polypeptide specifically
2 binds to antibodies generated against SEQ ID NO:4.

1 14. The polypeptide of claim 12, wherein the potassium channel
2 further comprises the characteristic of rapid activation.

1 25. The method of claim 24, wherein the functional effect is a physical
2 effect.

1 26. The method of claim 24, wherein the functional effect is a chemical
2 effect.

1 27. The method of claim 24, wherein the polypeptide is expressed in a
2 eukaryotic host cell or cell membrane.

1 28. The method of claim 27, wherein the functional effect is
2 determined by measuring ion flux, changes in ion concentrations, changes in current or
3 changes in voltage.

1 29. The method of claim 24, wherein the functional effect is
2 determined by measuring ligand binding to the channel.

1 30. The method of claim 24, wherein the polypeptide is recombinant.

1 31. The method of claim 24, wherein the potassium channel is
2 homomeric.

1 32. The method of claim 24, wherein the potassium channel is
2 heteromeric.

1 33. The method of claim 24, wherein the polypeptide has an amino
2 acid sequence of SEQ ID NO:4.

1 34. A method for identifying a compound that increases or decreases
2 ion flux through a potassium channel comprising a Slo4 polypeptide, the method
3 comprising the steps of:

4 (i) entering into a computer system an amino acid sequence of at least 25
5 amino acids of a Slo4 polypeptide or at least 75 nucleotides of a nucleic acid encoding the
6 Slo4 polypeptide, the Slo4 polypeptide comprising a subsequence having at least 60%
7 amino acid sequence identity to an amino acid sequence of SEQ ID NO:4;

8 (ii) generating a three-dimensional structure of the polypeptide encoded by
9 the amino acid sequence;

- 10 (iii) generating a three-dimensional structure of the potassium channel
- 11 comprising the Slo4 polypeptide;
- 12 (iv) generating a three-dimensional structure of the compound; and
- 13 (v) comparing the three-dimensional structures of the polypeptide and the
- 14 compound to determine whether or not the compound binds to the polypeptide.

1 35. A method of modulating ion flux through a Slo potassium channel

2 comprising a Slo4 polypeptide to treat disease in a subject, the method comprising the

3 step of administering to the subject a therapeutically effective amount of a compound

4 identified using the method of claim 24 or 34.

1 36. A method of detecting the presence of hSlo4 in human tissue, the

2 method comprising the steps of:

3 (i) isolating a biological sample;

4 (ii) contacting the biological sample with an hSlo4-specific reagent

5 that selectively associates with hSlo4; and,

6 (iii) detecting the level of hSlo4-specific reagent that selectively

7 associates with the sample.

1 37. The method of claim 36, wherein the hSlo4-specific reagent is

2 selected from the group consisting of: hSlo4-specific antibodies, hSlo4-specific

3 oligonucleotide primers, and hSlo4-nucleic acid probes.

1 38. In a computer system, a method of screening for mutations of a

2 human Slo4 gene, the method comprising the steps of:

3 (i) entering into the computer a first nucleic acid sequence

4 encoding a Slo4 polypeptide having an amino acid sequence of SEQ ID NO:4, and

5 conservatively modified versions thereof;

6 (ii) comparing the first nucleic acid sequence with a second nucleic

7 acid sequence having substantial identity to the first nucleic acid sequence; and

8 (iii) identifying nucleotide differences between the first and second

9 nucleic acid sequences.

1 39. The method of claim 38, wherein the second nucleic acid sequence

2 is associated with a disease state.

1 40. An isolated nucleic acid encoding a Slo2 polypeptide comprising
 2 an alpha subunit of a Slo potassium channel, the polypeptide:

3 (i) forming, with at least one additional alpha subunit, a potassium
 4 channel comprising the characteristic of voltage-gating; and

5 (ii) comprising an amino acid sequence of SEQ ID NO:2.

1 41. The nucleic acid of claim 40, wherein the potassium channel
 2 further comprises the characteristic of rapid activation.

1 42. The nucleic acid of claim 40, wherein the nucleic acid comprises a
 2 nucleotide sequence of SEQ ID NO:1.

1 43. An isolated nucleic acid encoding a Slo2 polypeptide, wherein the
 2 nucleic acid is amplified by primers that selectively hybridize under stringent
 3 hybridization conditions to the same sequence as the primers selected from the group
 4 consisting of:

5 5'-TTAGAGCTGTGTCTCGTCGCGAGTCTC-3' (14) (SEQ ID NO:18)

6 5'-ATGGCGCGGGCCAAGCT-3' (15) (SEQ ID NO:19)

7 5'-GAGACAGGGAGGAGTCCAGGCTGAA-3' (16) (SEQ ID NO:20)

8 5'-CGTGGGCCAGAGGCTTCCTGTAGAA-3' (17) (SEQ ID NO:21).

1 44. The nucleic acid of claim 40, wherein the polypeptide encoded by
 2 the nucleic acid comprises an alpha subunit of a homomeric potassium channel.

1 45. The nucleic acid of claim 40, wherein the polypeptide encoded by
 2 the nucleic acid comprises an alpha subunit of a heteromeric potassium channel.

1 46. A method of detecting a nucleic acid, the method comprising
 2 contacting the nucleic acid with an isolated nucleic acid of claim 40.

1 47. An isolated Slo2 polypeptide comprising an alpha subunit of a Slo
 2 potassium channel, the polypeptide:

3 (i) forming, with at least one additional Slo alpha subunit, a Slo
 4 potassium channel comprising the characteristic of voltage-gating; and

5 (ii) comprising a sequence having an amino acid sequence of SEQ
 6 ID NO:2.

59. The method of claim 58, wherein the functional effect is determined by measuring ion flux, changes in ion concentrations, changes in current or changes in voltage.

60. The method of claim 55, wherein the functional effect is determined by measuring ligand binding to the channel.

61. The method of claim 55, wherein the polypeptide is recombinant.

62. The method of claim 55, wherein the potassium channel is homomeric.

63. The method of claim 55, wherein the potassium channel is heteromeric.

64. A method for identifying a compound that increases or decreases ion flux through a potassium channel comprising a Slo2 polypeptide, the method comprising the steps of:

(i) entering into a computer system an amino acid sequence of SEQ ID NO:2;

(ii) generating a three-dimensional structure of the polypeptide encoded by the amino acid sequence;

(iii) generating a three-dimensional structure of the potassium channel comprising the Slo2 polypeptide;

(iv) generating a three-dimensional structure of the compound; and

(v) comparing the three-dimensional structures of the polypeptide and the compound to determine whether or not the compound binds to the polypeptide.

65. A method of modulating ion flux through a Slo potassium channel comprising a Slo2 polypeptide to treat disease in a subject, the method comprising the step of administering to the subject a therapeutically effective amount of a compound identified using the method of claim 55 or 64.

66. A method of detecting the presence of hSlo2 in human tissue, the method comprising the steps of:

(i) isolating a biological sample;

4 (ii) contacting the biological sample with an hSlo2-specific reagent
5 that selectively associates with hSlo2; and,
6 (iii) detecting the level of hSlo2-specific reagent that selectively
7 associates with the sample.

1 67. The method of claim 66, wherein the hSlo2-specific reagent is
2 selected from the group consisting of: hSlo2-specific antibodies, hSlo2-specific
3 oligonucleotide primers, and hSlo2-nucleic acid probes.

1 68. In a computer system, a method of screening for mutations of a
2 human Slo2 gene, the method comprising the steps of:

3 (i) entering into the computer a first nucleic acid sequence
4 encoding a Slo2 polypeptide having an amino acid sequence of SEQ ID NO:2, and
5 conservatively modified versions thereof;

6 (ii) comparing the first nucleic acid sequence with a second nucleic
7 acid sequence having substantial identity to the first nucleic acid sequence; and

8 (iii) identifying nucleotide differences between the first and second
9 nucleic acid sequences.

1 69. The method of claim 68, wherein the second nucleic acid sequence
2 is associated with a disease state.